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Maintenance Chemotherapy Versus Consolidative Stereotactic Body Radiation Therapy (SBRT) plus Maintenance Chemotherapy for Stage IV Non-Small Cell Lung Cancer (NSCLC): A Randomized Phase II Trial

Date 3/9/2016

The University of Texas Southwestern Medical Center
Parkland Health & Hospital System
Children's Medical Center
Retina Foundation of the Southwest
Texas Scottish Rite Hospital for Children
Texas Health Presbyterian Hospital Dallas

CONSENT TO PARTICIPATE IN RESEARCH

Title of Research:	Maintenance Chemotherapy Versus Consolidative Stereotactic Body Radiation Therapy (SBRT) plus Maintenance Chemotherapy For Stage IV Non-Small Cell Lung cancer (NSCLC): A Randomized Phase II Trial
Sponsor:	University of Texas Southwestern Medical Center at Dallas
Principal Investigator:	Puneeth Iyengar, MD, Ph.D 5801 Forest Park Road Dallas, Texas 75390-9183 214-645-8525

You may call the study doctors or research personnel at all times at 214-645-8525.

Instructions:
Please read this consent form carefully and take your time making a decision about whether to participate. As the researchers discuss this consent form with you, please ask him/her to explain any words or information that you do not clearly understand. The purpose of the study, risks, inconveniences, discomforts, and other important information about the study are listed below. If you decide to participate, you will be given a copy of this form to keep.

Why is this study being done?
This study is being done to compare the effects, good and/or bad of different types of chemotherapy with radiation therapy on you and your stage IV non-small cell lung cancer to find out which is better.

In this study, we are adding a specialized form of radiation treatment called stereotactic body radiation therapy (SBRT).

- SBRT is a highly precise form of radiation therapy used primarily to treat cancer
- SBRT is a non-surgical procedure that uses highly focused x-rays.
- SBRT has an acceptable toxicity with quicker recovery and limited delay
- SBRT is to improve tumor control while reducing the side effects.

- SBRT is currently under active investigation at numerous institutions worldwide.

All patients enrolled on this trial will receive 4-6 cycles of initial (first line) chemotherapy. After the initial chemotherapy, you will be randomized to either maintenance chemotherapy alone or SBRT followed by maintenance chemotherapy.

Why is this considered research?
This is a research study because we want to find out if SBRT prior to standard maintenance chemotherapy may provide further benefit over maintenance chemotherapy.

The following definitions may help you understand this study:

- Standard medical care means the regular care you would receive from your personal doctor if you choose not to participate in this research.
- Researchers means your doctor and research personnel at the University of Texas Southwestern Medical Center at Dallas and its affiliated hospitals.
- Randomization means you will be placed by chance (like a flip of a coin) in one of the study groups

Why am I being asked to take part in this research study?
You are being asked to take part in this study because you have stage IV non-small cell lung cancer.

Do I have to take part in this research study?"
No. You have the right to choose whether you want to take part in this research study. If you decide to participate and later change your mind, you are free to stop participation at any time.

If you decide not to take part in this research study it will not change your legal rights or the quality of health care that you receive at this center.

How many people will take part in this study?
About 36 people will take part in this study at UT Southwestern or Parkland Health & Hospital System.

What is involved in the study?
If you agree to be in this study, you will be asked to sign this consent form and will have the following tests and procedures done. These procedures are part of your standard medical care.

Screening Procedures

To help decide if you qualify to be in this study, you may also have to fill out certain forms or have the following exams, tests, or procedures:

- History and physical exam, the study doctor will ask you questions about your health, medications you take for any health problems, and any surgical procedures you have had.
- Performance status
- Blood Tests, approximately 2 tablespoons of blood will be taken to check levels of white blood cells, red blood cells, platelets in your body, and to check if your liver is working normally.
- Computed Tomography (CT) Scan of the chest, abdomen and/or pelvis as clinically indicated by your doctor. These are special scans that show computerized pictures of your chest and abdomen.
- Positron Emission Tomography (PET) Scan of the whole body or Magnetic Resonance Imaging (MRI).
- Smoking History Assessment, questions will be asked about your smoking history.

If the researchers believe you can take part in this study, you will be assigned randomly to either maintenance chemotherapy alone or SBRT followed by maintenance chemotherapy.

Study treatments

If you take part in the maintenance chemotherapy alone, you will be receiving standard drugs. Currently accepted drugs used for maintenance chemotherapy include Erlotinib, Pemetrexed, Docetaxel, Gemcitabine, and Bevacizumab. These drugs are standard of care and are commercially available

- Erlotinib (Tarceva):
  Tarceva® tablets should be taken at approximately the same time of day. Each Tarceva® dose is to be taken with up to 200 mL (~ 1 cup or 8 oz) of water, and should be taken 1 hour before or 2 hours after meals or medications, including grapefruit juice, vitamins, and iron supplements. The entire dose must be taken at one time. If you vomit after taking the tablet(s), the dose is replaced only if the tablet(s) can actually be seen and counted.

- Pemetrexed (Alimta)
  This will be giving as an intravenous infusion over 10 minutes on Day 1 of each 21-day cycle. To reduce toxicity, you will be instructed to take a low-dose oral folic acid preparation or multivitamin with folic acid on a daily basis. At least 5 daily doses of folic acid must be taken during the 7-day period prior to the first dose of Alimta; and continue during the full course of therapy and for 21 days after the last dose of Alimta. You will also receive one (1) intramuscular injection of vitamin B12 during the week prior to the first dose of Alimta and every 3 cycles thereafter. Subsequent vitamin B12 injections may be given the same day as Alimta.

- Docetaxel
  This will be giving as an intravenous infusion according to your physician's order.

- Gemcitabine (Gemzar)
  Gemzar will be given intravenously at one these two schedules (1)With the 4-week schedule, Gemzar will be given over 30 minutes on Days 1, 8, and 15 of each 28-day cycle; (2)With the 3-week schedule, Gemzar will be given 30 minutes on Days 1 and 8 of each 21-day cycle.

- Bevacizumab (Avastin)
  Avastin will be given intravenously according to your physician's order.

During the maintenance chemotherapy, you will have the following procedures:
- History and physical exam, the study doctor will ask you questions about your health, medications you take for any health problems, and any surgical procedures you have had.
- Performance status
- Blood Tests, approximately 2 tablespoons of blood will be taken to check levels of white blood cells, red blood cells, platelets in your body, and to check if your liver is working normally.
- Toxicities assessment

If you take part in the SBRT followed by maintenance chemotherapy, you will have a planning session called a simulation prior to SBRT treatment. This planning session is used to design your radiation treatments. You will be positioned in a stable position that allows accurate reproducibility of the target between treatments. A variety of immobilization systems may be used including stereotactic frames or large pillows.

Based on location of the metastatic lesion(s), radiation dose and number of treatment will be determined your doctor (radiation oncologist). You might get one, three, or five treatments. You may receive treatment on consecutive days with 18 hours between each treatment or every other day as deemed appropriate by your doctor.

During the SBRT, you will have the following procedures:

- Toxicities assessment

After the SBRT, you will receive standard maintenance chemotherapy and procedures as described above.

Follow-up procedures

You will have the following procedures:

- History and physical exam: at one month after SBRT, every 3 months for year 1, every 6 months for years 2-3, and every 12 months for years 4-5
- Performance status: at one month after SBRT, every 3 months for year 1, every 6 months for years 2-3, and every 12 months for years 4-5
- Blood Tests: approximately 2 tablespoons of blood will be taken at 3 months and 6 months after SBRT. Then as clinically indicated
- Toxicities assessment: at one month after SBRT, every 3 months for year 1, every 6 months for years 2-3, and every 12 months for years 4-5
- CT scan of chest, abdomen and/or pelvis as clinically indicated (CT) at 3 months and 6 months after SBRT, then as clinically indicated
- PET scan or MRI at 3 months and 6 months after SBRT if clinically indicated

How long can I expect to be in this study?

You will be followed for this study a minimum of 6 months. After 6 months, if you don't have progression disease, you will be followed every 3 months for year 1, every 6 months for years 2-3, and every 12 months for years 4-5. If your disease progressed, you will be followed every 3 months for year 1 and every 6 months for years 2-3

What are the risks of the study?

You may have side effects while on the study. Everyone taking part in the study will be watched carefully for any side effects. However, researchers don't know all the side effects that may happen. Side effects may be mild or very serious. Your health care team may give you medicines to help lessen side effects. Many side effects go away soon after you stop taking the radiation or chemotherapy. In some cases, side effects can be serious, long lasting, or may never go away.

Study Procedure/Intervention

Because of your participation in this study, you are at risk for the following side effects. You should discuss these with the researchers and your regular health care provider.

You may require an MRI:

There are no known risks from exposure to magnetic fields. You may experience nervousness and/or anxiety due to the loud banging made by the machine while it is taking pictures and from confinement in a tight space (claustrophobia). If you become anxious, you can stop the procedure at any time.

You may also experience some discomfort and fatigue from lying still during imaging.

If you have any metal clips or plates in your body, you should tell the investigator.

MRI may not be appropriate if you are pregnant or are trying to become pregnant. MRI may not be appropriate if you have permanent eyeliner or eyebrows or any pieces of metal in your body, such as the following:

- heart pacemaker, heart valve replacement, or aortic clips
- metal fragments in your eyes, skin, or elsewhere in your body
- brain clips or pieces of metal used in aneurysm surgery or intracranial bypass
- venous umbrella
- pieces of metal in the body resulting from work as a sheet-metal worker or welder
- clips placed in an internal organ
- prosthetic devices, such as middle ear, eye, joint, or penile implants
- joint replacement.
- hearing aid that cannot be removed
- neurostimulator
- insulin pump
- intrauterine device (IUD)
- shunts or stents
- metal mesh or coil implants
- metal plate, pin, screws, or wires, or any other metal implants.

For this study, if you have an MRI, you will receive a Contrast Agent.

The contrast agent you will receive is FDA-approved and used routinely for MRI exams. It contains a material called Gadolinium (dye solution used to highlight organs or tissues during imaging). The injection of Gadolinium may cause discomfort like headache, nausea, strange taste, or coldness at site of injection. These symptoms occur in less than 1 out of 20 patients receiving Gadolinium and go away quickly. There is a small risk of a severe allergic reaction that can cause breathing difficulties and/or low blood pressure, these symptoms are extremely rare (approximately 1 in 10,000 to 1 in 100,000 administrations). In the unlikely event you experience these symptoms, a physician and nursing staff will be available to evaluate and, if necessary, provide treatment. People with severe kidney failure who receive Gadolinium (dye used to highlight organs or tissues during imaging) are at risk of developing a disorder called Nephrogenic Systemic Fibrosis (NSF). This disease can cause wide spread tissue scarring or hardening (fibrosis). In rare cases NSF can lead to lung and heart problems and cause death. If you have severe kidney failure and receive gadolinium, the risk of developing NSF is 1-5%. We may perform a blood test 30 days before your MRI to check your how well your kidneys are working before you receive the Gadolinium. This

test may be repeated closer to your MRI appointment if your medical condition has changed. If your kidneys are working at levels known to be at risk for NSF, you will not receive Gadolinium. You will not receive Gadolinium for research purposes if you have either sickle cell disease (a disease of the blood cells) since it may put you at risk of developing hemolysis (breakdown of blood cells).

If you have a history of an implanted device or clips in your pelvis (involving your uterus or fallopian tubes) or under your skin, acting as a contraceptive to prevent pregnancy, the MRI technologists will obtain specific information about the make and model of your implanted device to determine if it is safe for you to receive the MRI examination.

Risks and side effects related to Erlotinib (Tarceva®):

More common Side Effects >10%

- Rash on face, neck, chest, back, and arms
- Diarrhea
- Loss of appetite
- Fatigue
- Conjunctivitis
- Tiredness
- Vomiting

Less Common Side Effects <10%

- Mild headache
- Sore mouth
- Shortness of breath
- Cough
- Abnormal liver function tests
- Dry skin
- Itching
- Infection associated with skin reactions
- Belly pain
- Nose bleeds
- Nail changes

Rare Side Effects <3%

- Inflammation of the cornea in the eye
- Puncture of the cornea
- Gastrointestinal bleeding
- Blistering and sloughing of the skin or gut lining which can be life-threatening
- Painful redness or peeling of the skin on the palms of the hands and soles of the feet
- Liver failure that can be life threatening or fatal, particularly in patients with underlying impairment of the liver function.

Risks and side effects related to Gemcitabine (Gemzar):

More common Side Effects >10%

- Lower blood counts, which can lead to a risk of infection and bleeding
- Nausea and/or vomiting
- Fatigue

Less Common Side Effects <10%

- Skin rash
- Constipation
- Diarrhea
- Fever
- Hair loss
- Pain
- Swelling
- Shortness of breath
- Sores in the mouth

Rare Side Effects <3%

- Decrease in liver function resulting in abnormal blood tests or jaundice (a yellowish color of the skin, tissues, and certain body fluids)
- Decrease in the kidneys' ability to handle the body's waste, which may be permanent
- Pneumonia

Risks and side effects related to Pemetrexed (Alimta)**:**

More common Side Effects >10%

- Black, tarry stools
- Bleeding gums
- Chest pain
- Chills
- Cough
- Loss of coordination
- Lower back or side pain
- Painful or difficult urination
- Pains in the chest, groin, or legs, especially calves of the legs
- Pale skin

Less Common Side Effects <10%

- Loss of coordination
- Pinpoint red spots on the skin
- Severe headaches of sudden onset
- Sore throat
- Unusual tiredness or weakness
- Nausea
- Skin rash
- Swelling of the eyes or eyelids
- Swelling of the face, fingers, or lower legs
- Vomiting

Rare Side Effects <3%

- Pale skin, easy bruising or bleeding, unusual weakness;
- Fever, chills, body aches, flu symptoms;
- White patches or sores inside your mouth or on your lips;
- Urinating less than usual, or not at all;
- Chest pain, trouble breathing;
- Swelling, rapid weight gain.
- Sudden onset of slurred speech
- Sudden vision changes
- Swollen glands
- Shortness of breath
- Vomiting

Risks and side effects related to Docetaxel:

Likely (>10%)

- Lowering of blood counts leading to increased risk of infection, weakness, or bleeding, which in rare cases could have fatal complications
- Hair loss
- Skin rash
- Changes to the nail beds
- Loss of appetite
- Taste changes
- Mouth sores
- Nausea and vomiting
- Diarrhea
- Constipation
- Fatigue
- Muscle aches and/or joint pain
- Decreased sensation, numbness, or tingling in the fingers and toes

Less Likely (<3-9%)

- Sweating
- Fever and chills
- Headache
- Weight gain
- Muscle cramps
- Hives
- Local skin reactions
- Flushing
- Ulcers of the stomach or esophagus
- Abdominal pain
- Increased tearing
- Reactions of the infusion site that include redness of the skin, dryness of the skin, mild swelling of the vein, changes in skin color, leakage of IV solution into the skin

Rare but Serious (<3%)

- Decreased vision, vision changes, or eye irritation
- Glaucoma and/or cataracts
- Dizziness
- Depression
- Seizures
- Confusion
- Muscle weakness
- Swelling in arms and legs
- Irritation of skin at sites of prior radiation
- Damage to skin at the site of injection in the vein
- Slow wound healing
- Blood in urine
- Allergic reaction including skin rash and difficulty breathing
- Low blood pressure
- Risk of developing leukemia requiring treatment
- Chest pain
- Slowing or irregular heart rhythm
- Heart damage, possibly including changes in rhythm and poor pumping of blood
- Liver and kidney damage
- Fluid build-up in the lungs
- Death from infection
- Bleeding into the stomach and/or intestines
- Obstruction of the intestines
- Changes in sensation in the nerves of the hands and feet
- Pulmonary embolism (a blockage of an artery in the lung)

Risks and side effects related to Bevacizumab (Avastin)**:**

More common Side Effects >10%

- Loss of the normal functioning of the ovaries in a woman that can result in temporary or permanent menopause; the impact on fertility (temporary or permanent) is unknown
- High blood pressure

Less Common Side Effects <10%

- anemia
- Fast heartbeat
- Feeling of spinning or whirling
- Inflammation (swelling and redness) of the large bowel (colon)
- Constipation
- Diarrhea
- Heartburn
- Bleeding and blockage in parts of the digestive tract
- Irritation or sores in the lining of the mouth
- Nausea /Vomiting
- Fatigue or tiredness
- Fever, chills, rash, low blood pressure, and difficulty breathing.
- Chest pain not heart-related
- Hives, low blood pressure, wheezing, swelling of the throat, and difficulty breathing.
- Infection
- Infection (collection of pus) around the rectum
- Premature opening of a wound along surgical stitches after surgery
- Increased blood level of a liver enzyme (ALT/SGPT)
- Increased blood level of a liver or bone enzyme (alkaline phosphatase)
- Increased blood level of a liver pigment (bilirubin) often a sign of liver problems
- Increased blood level of a heart muscle protein (troponin I) indicating damage to the heart muscle
- Decreased number of a type of white blood
- Weight loss/ Loss of appetite
- Joint pain/ Muscle pain
- Destruction or breakdown of jawbone
- Dizziness (or sensation of lightheadedness, unsteadiness, or giddiness)
- Headache or head pain
- Inflammation
- Fainting
- Blood in the urine
- kidney disease
- Bleeding in the vagina

- Stuffy or runny nose, sneezing
- Cough
- Shortness of breath
- Nose bleed
- Hoarseness
- Skin rash / Hives
- Formation of a blood clot

Rare Side Effects <3%

- Heart failure
- Ventricular fibrillation
- Sore (ulcer) somewhere in the digestive tract
- Extremely low blood pressure, swelling of the throat, difficulty breathing, and loss of consciousness.
- Leakage from stomach
- Bleeding in the brain
- Stroke
- headache, confusion, seizures, and vision loss
- Sudden decrease of kidney function
- Abnormal hole between part of the urinary system and another organ or tissue
- Abnormal hole between the vagina and another organ or tissue
- Bleeding from the lungs
- Hole in the wall that separates the nostrils of the nose
- Abnormal hole between the breathing tube (windpipe)
- Blockage or narrowing of a blood vessel

Reproductive risks: You should not become pregnant or father a baby while on this study because the drugs in this study can affect an unborn baby. If you are a woman of childbearing age, and have not been surgically sterilized (tubal ligation or hysterectomy), you must have a pregnancy test before enrolling in this study. Women must not breastfeed a baby while on this study. It is important you understand that you need to use birth control while on this study.

Because bevacizumab remains in your body for weeks to months, you should continue to use adequate birth control and avoid nursing a baby for at least 6 months after your last dose of bevacizumab although the exact time required for drug clearance cannot be precisely predicted.

Check with your research doctor about what kind of birth control methods to use and how long to use them. Some methods might not be approved for use in this study such as the rhythm method of birth control. Two forms of contraception are recommended, such as a combination of barrier (for example, a condom) and oral contraceptive pill.

For more information about risks and side effects, ask your study doctor.

Stereotactic Body Radiation Therapy (SBRT): The possible side effects of radiation therapy depend on where the cancer to be treated is located within the body. The most common possible side effects are discussed in the following sections. The most common parts of the body to be treated with SBRT are the liver and lung and possible side effects in these areas are mentioned separately.

Possible reactions regardless of what part of the body is treated:
Common (>10% chance):

- Weakness or fatigue

Uncommon (<10% chance):

- Sunburn-like skin changes near the tumor location (redness, irritation, scaliness)
- Skin reactions are more common, though, if the tumor to be treated is located very close to the skin. You can ask your doctor whether this condition applies in your case.
- Upset stomach, vomiting, loss of appetite, or altered sense of taste

Possible reactions if the tumor to be treated is in the liver:
Common (>10% chance)

- Temporary inflammation of the liver seen on CT scan or MRI or detected by blood tests

Rare (<1% chance)

- Significant loss of the function of the liver

Possible reactions if the tumor to be treated is in the lung:
Common (>10% chance)

- Mild to moderate discomfort in the chest wall near the tumor, sometimes requiring non-prescription or prescription pain relievers. This effect usually occurs a few weeks after the SBRT and goes away within a few weeks after it develops.
- Scar tissue formation in the lung seen on CT scan.

Uncommon (<10% chance)

- Inflammation of the lung, also called pneumonitis, requiring anti-inflammatory medicine called steroids
- Moderate loss of function of the lung. If you do not currently require supplemental oxygen but your lungs have already been affected by the cancer or prior treatment for it, you might need to begin using supplemental oxygen. If you already require supplemental oxygen, your needs might increase.

Rare (<1% chance)

- Significant loss of the function of the lung, including collapse of a lung or a large part of a lung.

Other possible reactions, depending upon which part of the body is treated*:*
Uncommon (<10% chance)

- Increased risk of bone fracture, if the tumor treated is in a bone or is near a bone, including the ribs.

Rare (<1% chance)

- Significant injury to the stomach or intestines, if the tumor is near these structures. There will be strict limits in the dose received by the spinal cord to minimize this risk.

Extremely rare (<1 in 1000)

- Spinal cord injury, if the tumor is near the spinal cord. There will be strict limits in the dose received by the spinal cord to minimize this risk.

Risks and side effects associated with radiation therapy include:

Site	Short term effects	Long term effects
Lung	1. Skin changes: redness, irritation, scaliness, ulceration, coloration, thickening, hair loss. 2. Inflammation of esophagus causing pain on swallowing, heartburn, or sense of obstruction. 3. Loss of appetite, nausea, vomiting. 4. Weight loss, weakness, vomiting. 5. Inflammation of the lung with pain, fever, and cough. 6. Inflammation of the heart sac with chest pain and palpitations. 7. Bleeding or creation of a fistula resulting from tumor destruction. 8. Depression of blood counts leading to increased risk of infections and/or bleeding 9. Intermittent electric shock-like feelings in the lower spine or legs on bending the neck.	1. Changes in skin texture and/or coloration, permanent hair loss, and scarring of the skin. 2. Lung scarring or shrinkage causing shortness of breath. 3. Narrowing of esophagus causing swallowing problems. 4. Constriction of heart sac which may require surgical correction 5. Damage to heart muscle or arteries leading to heart failure. 6. Fracture of ribs. 7. Nerve damage causing pain, loss of strength or feeling in arms. 8. Spinal cord damage causing loss of strength or feeling in arms and legs and/or loss of control of bladder and rectum.

Risks to an Embryo, Fetus or Breast-fed Infant

Females: If you are part of this study while pregnant or breast-feeding an infant, it is possible that you may expose the unborn child or infant to risks. For that reason, pregnant and breast-feeding females cannot participate in the study. If you can become pregnant, a blood pregnancy test will be done (using 1 teaspoon of blood drawn from a vein by needle-stick), and it must be negative before you can participate in this study. If you take part in this study and are sexually active, you and any person that you have sex with must use medically-acceptable birth control (contraceptives) during the study. Medically-acceptable birth control (contraceptives) includes:

- Surgical sterilization (such as hysterectomy or "tubes tied"),
- Approved hormonal contraceptives (such as birth control pills, patch or ring; Depo-Provera, Depo-Lupron, Implanon),
- Barrier methods (such as condom or diaphragm) used with a spermicide (a substance that kills sperm), or
- An intrauterine device (IUD).

If you do become pregnant during this study, you must tell the researchers immediately.

Radiation exposure to a woman's reproductive organs may harm an embryo or fetus. Also, if radioactive materials are used for certain types of scans, harm may come to an embryo, fetus, or an infant who is breast feeding.

Pregnancy tests performed during the early stages of pregnancy do not always reveal pregnancy. Therefore, radiation exposure that includes the reproductive organs will be limited to the first ten days after a woman of child bearing potential has begun her most recent menstrual period. This is standard policy in clinics and hospitals within UT Southwestern. This policy applies unless there is an important medical reason requiring radiation outside this time frame.

Males: Being in this research may damage your sperm which could cause harm to a child that you may father while on this study. If you take part in this study and are sexually active, you must agree to use a medically-acceptable form of birth control. Medically-acceptable forms of birth control include:

- Surgical sterilization (vasectomy), or
- A condom used with a spermicide (a substance that kills sperm).

Risks of Radiation – Diagnostic Test

The radiation dose that you will get from diagnostic tests is medically indicated for your condition and it is the same that you would get if you were not involved in this research study.

Risks of Blood Drawing
Risks associated with drawing blood from your arm include minimal discomfort and/or bruising. Infection, excess bleeding, clotting, and/or fainting also are possible, although unlikely. You will have the same amount of blood collected whether you receive standard medical care for your health problem or take part in this research.

Psychological Stress includes those which are:
Some of the questions we will ask you as part of this study may make you feel uncomfortable. You may refuse to answer any of the questions, take a break or stop your participation in this study at any time.

Other Risks
There may possibly be other side effects that are unknown at this time. If you are concerned about other unknown side effects, please discuss this with the researchers.

Loss of Confidentiality
Any time information is collected; there is a potential risk for loss of confidentiality. Every effort will be made to keep your information confidential; however, this cannot be guaranteed.

How will risks be minimized or prevented?
During your participation in this research, your study doctor will watch you closely to determine whether there are problems that need medical care. If a device or belt is used to control tumor movements during your SBRT treatments, a hospital staff or physician will be watching you at all time to monitor your breathing pattern and to be available should you have any complaints or discomforts.
Before you receive your SBRT treatments, you will be place on the treatment table with the device of belt attach just as you would during treatment and a CT scan will be obtain. This CT scan will also let your physician know if the device or belt is making it difficult to breathe.

What will my responsibilities be during the study?
While you are part of this study, the researchers will follow you closely to determine whether there are problems that need medical care. It is your responsibility to do the following:

- Ask questions about anything you do not understand.
- Keep your appointments.
- Follow your doctor's instructions.
- Let your doctor know if your telephone number or address changes.
- Store all study drugs in a secure place at home away from anyone who is unable to read and understand labels, especially children.
- Tell your doctor before you take any new medication, even if it is prescribed by another doctor for a different medical problem or something purchased over the counter.
- Tell your doctor about your participation in this study.
- Carry information about your medication in your purse or wallet.

Report to your doctor any injury or illness while you are on study even if you do not think it is related

If I agree to take part in this research study, will I be told of any new risks that may be found during the course of the study?
Yes. You will be told if any new information becomes available during the study that could cause you to change your mind about continuing to participate or that is important to your health or safety.

What should I do if I think I am having problems?
If you have unusual symptoms, pain, or any other problems while you are in the study, you should report them to your doctor and the researchers right away. Telephone numbers where they can be reached are listed on the first page of this consent form.

If you have a sudden, serious problem like difficulty breathing or severe pain, go to the nearest hospital emergency room or call 911 (or the correct emergency telephone number in your area). Tell emergency personnel about any medications you are taking, including any medications you are taking for this study.

What are the possible benefits of this study?
If you agree to take part in this study, there may or may not be direct benefits to you. The researchers cannot guarantee that you will benefit from participation in this research.

We hope the information learned from this study will benefit others with lung cancer in the future. Information gained from this research could lead to better understanding of stage IV non-small cell lung cancer treatment.

What options are available if I decide not to take part in this research study?
You do not have to participate in this research to receive care for your medical problem. Instead of being in this study, you have the following options:

- Receive standard treatment depending on the treating physician's assessment.
- Taking part in another study
- Getting no treatment

Please talk to the researchers or your personal doctor about these options..

Will I be paid if I take part in this research study?
No. You will not be paid to take part in this research study. There are no funds available to pay for parking expenses, transportation to and from the research center, lost time away from work and other activities, lost wages, or child care expenses.

Will my insurance provider or I be charged for the costs of any part of this research study?
No. Neither you, nor your insurance provider, will be charged for anything done only for this research study (i.e., the Screening Procedures, Experimental Procedures, or Monitoring/Follow-up Procedures described above).

However, the standard medical care for your condition (care you would have received whether or not you were in this study) is your responsibility (or the responsibility of your insurance provider or governmental program). You will be charged, in the standard manner, for any procedures performed for your standard medical care.

What will happen if I am harmed as a result of taking part in this study?
It is important that you report any illness or injury to your doctor immediately. Compensation for an injury resulting from your participation in this research is not available from the University of Texas Southwestern Medical Center at Dallas and Parkland Health & Hospital System.

You retain your legal rights during your participation in this research.

Can I stop taking part in this research study?
Yes. If you decide to participate and later change your mind, you are free to stop taking part in the research study at any time.

If you decide to stop taking part in this research study, it will not affect your relationship with the UT Southwestern staff or doctors. Whether you participate or not will have no effect on your legal rights or the quality of your health care.

Your doctor is a research investigator in this study. S/he is interested in both your medical care and the conduct of this research study. At any time, you may discuss your care with another doctor who is not part of this research study. You do not have to take part in any research study offered by your doctor.

If I agree to take part in this research study, can I be removed from the study without my consent?
Yes. The researchers may decide to take you off this study if:

- Your medical problem remains unchanged or becomes worse.
- The researchers believe that participation in the research is no longer safe for you.
- The Investigator decides to remove you from the research.
- The sponsor or the FDA stops the research for the safety of the participants.
- The sponsor cancels the research.
- You are unable to keep appointments or to follow the researcher's instructions.

Will my information be kept confidential?
Information about you that is collected for this research study will remain confidential unless you give your permission to share it with others, or as described below. You should know that certain organizations that may look at and/or copy your medical records for research, quality assurance, and data analysis include:

- Representatives of government agencies, like the U.S. Food and Drug Administration (FDA), involved in keeping research safe for people; and
- The UT Southwestern Institutional Review Board.

A description of this clinical trial will be available on http://www.clinicaltrials.gov, as required by the U.S. Law. This Web site will not include information that can identify you. At most, the Web site will include a summary of the results. You can search this Web site at any time.

In addition to this consent form, you will be asked to sign an "Authorization for Use and Disclosure of Protected Health Information." This authorization will give more details about how your information will be used for this research study, and who may see and/or get copies of your information.

Is there anything else I should know before I decide?
Dr. Gerber has financial interest in companies who make medications used in this study. You should feel free to ask questions about this.

Are there procedures I should follow after stopping participation in this research?
Yes. You can decide to stop at any time. Tell the study doctor if you are thinking about stopping or decide to stop. He or she will tell you how to stop safely. It is important to tell the study doctor if you are thinking about stopping so any risks from the treatment can be evaluated by him/her. Another reason to tell your study doctor that you are thinking about stopping is to discuss what follow-up care and testing could be most helpful for you.

The study doctor may stop you from taking part in this study at any time if he/she believes it is in your best interest; if you do not follow the study rules; or if the study is stopped.

Whom do I call if I have questions or problems?
For questions about the study, contact Puneeth Iyengar, MD at 214-645-8525 during regular business hours. For questions about your rights as a research participant, contact the UT Southwestern Institutional Review Board (IRB) Office at 214-648-3060.

SIGNATURES:
YOU WILL BE GIVEN A COPY OF THIS CONSENT FORM TO KEEP.

Your signature below certifies the following:

- You have read (or been read) the information provided above.
- You have received answers to all of your questions and have been told who to call if you have any more questions.
- You have freely decided to participate in this research.
- You understand that you are not giving up any of your legal rights.
- You understand that a copy of this signed consent document, information about this study and the results of any test or procedure done may be included in your medical record and this information may be available to health care providers and authorized persons including your insurance company.

_____ _____
Participant's Name (printed) Date Time am/pm

_____
Participant's Signature

_____ _____
Legally Authorized Representative's Name (printed) Date Time am/pm

_____
Legally Authorized Representative's Signature

_____ _____
Name of person obtaining consent (printed) Date Time am/pm

_____
Signature of person obtaining consent

INTERPRETER STATEMENT:

I have interpreted this consent form into a language understandable to the participant and the participant has agreed to participate as indicated by their signature above.

_____
Name of Interpreter (printed)

_____ _____
Signature of Interpreter Date time am/pm